

**REMARKS**

Claims 93-120 are pending in the application. Claims 1-92 have been canceled without prejudice. New claims 93-120 have been added. The right to prosecute the subject matter of any canceled claim in one or more continuation, continuation-in-part or divisional applications is hereby reserved. No new matter has been added.

Support for the new claims can be found, for example, in the table below.

Claim	Support
93	Page 6, lines 19-27; Page 10, lines 11-13; Page 18, lines 10-13, 19-21; Page 21, lines 9-10; Page 24, lines 7-14; Page 35, lines 11-16; Page 37, lines 5-9; Figures 3, 5-8
94	Page 24, lines 11-12
95	Page 24, line 12
96	Page 24, lines 12-13
97	Page 24, line 13
98	Page 13, line 10
99	Page 13, lines 10-15
100	Page 14, lines 1-7
101	Page 18, lines 10-11, 19-22; Page 35, lines 11-16; Page 37, lines 5-9
102	Page 19, lines 1-4
103	Page 19, lines 1-4
104	Page 19, lines 1-4
105	Page 19, lines 1-4
106	Page 1, lines 4-9, 24-25; Page 11, lines 23-27; Page 18, lines 10-11, 19-21; Page 23, lines 15-18; Page 26, lines 11-18; Page 27, lines 1-2; Abstract
107	Page 24, lines 11-12
108	Page 24, line 12
109	Page 24, lines 12-13

110	Page 24, line 13
111	Page 1, lines 24-25; Page 26, lines 15-18
112	Page 13, line 10
113	Page 13, lines 10-15
114	Page 14, lines 1-7
115	Page 18, lines 10-11, 19-22; Page 35, lines 11-16; Page 37, lines 5-9
116	Page 19, lines 1-4
117	Page 19, lines 1-4
118	Page 19, lines 1-4
119	Page 19, lines 1-4
120	Page 26, lines 24-26

#### Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 22-33 and 49-92 have been rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Without conceding the merits of the § 112, second paragraph rejection, claims 22-33, 49-75, 77-89, and 92 have been canceled without prejudice, rendering the rejection of these claims moot.

Furthermore, none of new claims 93-120 recites the language “solubility of the second amphiphilic component ---- is at least ten times greater than the solubility of the first amphiphilic lipid component,” “further selected such that the permeation capability of the vesicles increases disproportionately or nonlinearly under increasing pressure,” “for example,” “which are smaller than the constrictions in the barrier,” “communuting,” or “after the liquid droplets have formation.” Also, no new claim recites chemical moieties as amphiphilic lipids.

In view of the cancellation without prejudice of claims 22-33, 49-75, 77-89, and 92, and the fact that the presently pending claims do not recite the above-quoted language, it is believed that the presently pending claims meet the requirements of 35 U.S.C. § 112, second paragraph.

Consequently, it is believed that the rejection of claims 22-33, 49-75, 77-89, and 92 under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

### **Double Patenting Rejections**

Claims 53-75 and 77-89 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-35 of U.S. Patent No. 6,165,500 (the “‘500 patent”). Without conceding the merits of the obviousness-type double patenting rejection, claims 53-75 and 77-89 have been canceled without prejudice, rendering the rejection of these claims moot.

Furthermore, the presently pending claims are patentably distinct from the claims of the ‘500 patent because, as explained below, the claims of the ‘500 patent do not teach or suggest the particular vesicular compositions recited in the presently pending claims.

Presently pending independent claim 93 and its dependent claims 94-120 relate to a vesicular composition comprising an aqueous medium and a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic non-steroidal anti-inflammatory drug (NSAID) surfactants. In stark contrast, claim 1 and dependent claims 2-35 of the ‘500 patent relate to a method for transporting medical agents comprising applying transfersomes that comprise a lipid and a surfactant, and that have a medical agent associated with them. None of claims 1-35 of the ‘500 patent suggests, much less teaches, an NSAID surfactant, still less an amphiphilic NSAID surfactant, and even less a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants. Furthermore, even if the medical agent of the claims of the ‘500 patent were an NSAID, the claims of the ‘500 patent would still relate to transfersomes comprising a surfactant *in addition* to the NSAID medical agent. In contrast to the transfersomes of the claims of the ‘500 patent, the vesicles of the presently claimed compositions are useful for transporting an NSAID through human or animal skin or mucous membranes *even in the absence of a non-NSAID surfactant*.

In view of the above, it is believed that the presently pending claims are patentably distinct from the claims of the ‘500 patent. Therefore, it is believed that the rejection under the judicially created doctrine of obviousness-type double patenting over the ‘500 patent has been overcome and should be withdrawn.

Claims 22-33, 49-75 77-89, and 92 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 69-87 and 101-103 of copending U.S. Patent Application No. 10/357,618 (the “‘618 application”). Without conceding the merits of the provisional double patenting rejection, claims 22-33, 49-75 77-89, and 92 of the present application have been canceled without prejudice, rendering the rejection of these claims moot.

Furthermore, the presently pending claims are patentably distinct from claims 69-87 and 101-103 of the ‘618 application. Presently pending independent claim 93 and its dependent claims 94-120 relate to a vesicular composition comprising a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants. In stark contrast, the claims of the ‘618 application relate to aggregates comprising a first, a second, and a third amphiphilic component. None of claims 69-87 or 101-103 of the ‘618 application suggests, much less teaches, a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants. In contrast to the claims of the ‘618 application, the present claims relate to compositions that are useful for transporting an NSAID through porous barriers such as human or animal skin or mucous membranes *even in the absence of a third amphiphilic component.*

In view of the above, it is believed that that the presently pending claims are patentably distinct from claims 69-87 and 101-103 of the ‘618 application. Therefore, it is believed that the rejection under the judicially created doctrine of obviousness-type double patenting over claims 69-87 and 101-103 of the ‘618 application has been overcome and should be withdrawn.

For the reasons above, it is respectfully requested that the rejections under the judicially created doctrine of obviousness-type double patenting be withdrawn.

#### Rejections Under 35 U.S.C. §102(b)

Claims 22-30, 32, 49-50, and 92 have been rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Blume, et al., Journal of Liposome Research, 2(3): 355-368, 1992 (“Blume”). Without conceding the merits of the § 102(b) rejection, claims 22-30, 32, 49-50, and 92 have been canceled without prejudice, rendering the rejection of these claims moot.

Furthermore, Blume does not anticipate the presently pending claims 93-120. As the office action notes, nowhere does Blume disclose an NSAID. In stark contrast, pending claim 93 and dependent claims 94-120 recite a vesicular composition comprising an aqueous medium and a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants. It is therefore believed that Blume does not anticipate the presently pending claims and the rejection under 35 U.S.C. § 102(b) over Blume has been overcome and should be withdrawn.

Claims 22-33, 49-75, 77-89, and 92 have been rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by EP 0 475 160, of which the '500 patent is an English equivalent. Without conceding the merits of the § 102(b) rejection, claims 22-33, 49-75, 77-89 and 92 have been canceled without prejudice, rendering the rejection of these claims moot.

Furthermore, as discussed herein, the presently pending claims 93-120 are not anticipated by the '500 patent. The '500 patent discloses NSAIDs only in the context of a medical agent that is associated with the transfersome's lipid and surfactant. As discussed above, the '500 patent does not disclose a vesicular composition comprising a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants.

In view of the above, it is believed that the rejections of the claims under 35 U.S.C. § 102(b) as being anticipated by Blume EP 0 475 160 have been overcome and should be withdrawn.

#### Rejection Under 35 U.S.C. §103(a)

Claims 22-33, 49-75, 77-89, and 92 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over EP 0 475 160, of which the '500 patent is an English language equivalent. In addition, claims 24-25, 31, 51-52, 68-75, 77-89, and 92 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Blume in view of EP 0 475 160. Without conceding the merits of the § 103(a) rejection, claims 22-33, 49-75, 77-89, and 92 have been canceled without prejudice, rendering these rejections moot

Furthermore, the '500 patent does not render obvious the presently pending claims, either alone or in combination with Blume, for the reasons discussed herein. As stated above, the '500 patent relates to transfersomes comprising a lipid and a surfactant and being associated with a medical agent. Also, as stated above, the '500 patent does not teach or suggest the use of a

vesicular composition comprising a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants, which the presently pending claims recite. Blume does not cure the deficiency of the '500 patent because, as the office action notes, nowhere does Blume disclose an NSAID. In addition, nowhere does Blume teach or suggest an amphiphilic NSAID surfactant or the use of vesicles containing an amphiphilic NSAID surfactant. In stark contrast to Blume, the presently pending claims recite a vesicular composition comprising an aqueous medium and a vesicle consisting essentially of one or more phosphatidyl cholines and one or more amphiphilic NSAID surfactants.

The Examiner's attention is invited to **FIG. 8** of the present application. **FIG. 8** compares the permeation capability of Comparison Examples A-E, which are transfersomes that comprise a lipid and a non-NSAID surfactant and some of which are further associated with a medical agent, with the permeation capability of an illustrative vesicle of the present pending claims, which consists essentially of phosphatidyl choline from soy beans and ibuprofen, such as disclosed in Examples 18-25. **FIG. 8** shows that vesicles consisting essentially ibuprofen, an illustrative amphiphilic NSAID surfactant, and phosphatidyl choline from soy beans show a significantly higher permeation capability than Comparison Examples A-E, *even in the absence of a non-NSAID surfactant*. Therefore, illustrative vesicular compositions of the present claims have superior barrier permeation capability to Comparison Examples A-E.

In light of the above, it is believed that the presently pending claims are not obvious over the '500 patent, either alone or in combination with Blume. Therefore, it is respectfully requested that the rejection of the claims as being unpatentable under 35 U.S.C. § 103(a) over the '500 patent, either alone or in combination with Blume, be withdrawn.

Conclusion

It is respectfully requested that the Examiner enter the present amendment in light of the foregoing remarks and it is believed that all the claims are in condition for allowance. If the Examiner believes that a telephone interview would help expedite the successful prosecution of the claims, the undersigned attorney would be grateful for the opportunity to discuss any issues.

Please charge any payments due to Wilmer Cutler Pickering Hale and Dorr LLP Deposit Account No. 08-0219.

Respectfully submitted,  
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Date: January 5, 2007

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